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ANNALS OF PHYSICAL MEDICINE

The Official Organ of the
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ORIGINAL PAPER

LABORATORY INVESTIGATIONS IN THE DIAGNOSIS OF RHEUMATIC DISEASES

By J. H. GLYN and MARY IRVING

From the Department of Physical Medicine and Rheumatism, Prince of Wales Hospital, Tottenham, and Edgware General Hospital, London

It is becoming increasingly apparent that the erythrocyte sedimentation rate (E.S.R.) can be a fallible guide when used for the purpose of screening and sorting patients who attend rheumatism clinics complaining of ill-defined symptoms (Ansell and Bywaters, 1958; Shannon and Bywaters, 1957). There are now available a large number of non-specific "acute-phase" serological tests—i.e. tests indicative of acute inflammatory disease—whose value in general runs parallel to that of the E.S.R. The clinical usefulness of these reactions has been studied in relation to long-term steroid therapy (Glyn, 1956). Unfortunately they proved to be unreliable and their routine use for this particular purpose could not be recommended. In two respects, however, they were consistent. First, it was found before treatment that in every patient whose disease was clinically active all the tests showed levels significantly above the range of normal controls. Secondly, whereas some of the reactions appeared to be very labile and to fluctuate quickly in response to small clinical changes, others remained obstinately raised, and reflected major rather than trivial changes in disease activity. It was therefore decided to apply a group of similar tests to the diagnostic problems involved in sorting significant from prognostically insignificant rheumatic disease. The opportunity was also taken to evaluate them as a measurement of disease activity in established disease.

TABLE I

TESTS AND METHODS, AND LIMIT OF NORMAL VALUES

Test	Method	Upper Limit of Normal (mean ± twice standard deviation)	
		Male	Female
Erythrocyte sedimentation rate (E.S.R.)	Westergren (1926)	10 mm. in first hour	20 mm. in first hour
C-reactive protein (C.R.P.)	Wood and McCarty (1951)	0-½ unit (range 0-4 units)	0-½ unit (range 0-4 units)
Total protein-bound polysaccharides (glycoproteins—T.P.P.)	Rimington (1940)	185 mg. per 100 ml.	181 mg. per 100 ml.
Mucoprotein polysaccharides (seromucoids—M.P.)	Winzler *et al.** (1948)	19·1 mg. per 100 ml.	17·8 mg. per 100 ml.
Total protein (T.P.)	Weichselbaum (1946)	8·6 g. per 100 ml.	8·9 g. per 100 ml.
Protein : polysaccharides ratio (P : P) $\frac{\text{T.P.P.} \times 100}{\text{T.P.} \times 1000}$	Payne *et al.* (1955)	2·61	2·47

* The final estimation of the separated mucoproteins was carried out by the orcinol method of Rimington.

TABLE II

CLASSIFICATION

Disease	Number of Cases	Sex Distribution		Total Tests Performed
		Males	Females	
Rheumatoid arthritis	125 (disease active in 91)	65	60	166
Ankylosing spondylitis	23 (disease active in 14)	17	6	32
"Observations" (rheumatoid arthritis and ankylosing spondylitis)	77	36	41	114
Osteoarthritis	18	9	9	32
Non-articular rheumatism (including psychogenic rheumatism)	8	0	8	12
Miscellaneous cases (mainly suspected collagen disorders) ..	26	7	19	32
Normal control cases	53	28	25	67
Total	330	162	168	455

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TESTS USED AND MATERIAL

In selecting the tests two criteria were employed: (1) claims as to their clinical usefulness must already have been made by other workers; and (2) each one had to be sufficiently simple for routine clinical use if it proved of value. Table I lists the tests which were finally selected as fulfilling these criteria, the methods employed, and the upper limits of normal values for the tests.

Altogether 330 patients were examined in the course of the study, and since many of them were tested repeatedly a total of 455 comprehensive studies were made. The patients can conveniently be classified into the seven groups shown in Table II.

Of the 125 patients with rheumatoid arthritis, 91 were considered to have definitely active disease, and clinical activity was assessed on a 0–4 scale each time their blood was drawn. Grade 0 was inactive, Grade 1 was considered to be of doubtful activity, whereas patients classified as Grade 4 had fulminating activity and rapid deterioration (see Table VI for full classification). Only 14 out of 23 patients with ankylosing spondylitis were considered to have active disease. There were 77 patients whose condition was undiagnosable when they were first seen, but in whom a suspicion of incipient rheumatoid arthritis or ankylosing spondylitis was present. It is in these cases that the *diagnostic* usefulness of these tests could properly be evaluated, whereas from the other groups their accuracy in measuring disease activity could be assessed.

RESULTS

(1) Patients with Anomalous E.S.R.s

Table III demonstrates the relative reliability of the E.S.R. and the new tests. It concerns exclusively those cases in which the E.S.R. reading was inconsistent with the clinical picture. It will be seen that the relative figures for anomalies in rheumatoid arthritis are 30%* for the E.S.R. compared with 3·5% for the other tests, and for ankylosing spondylitis 7% as opposed to 0 respectively.

In the group in which the E.S.R. was unexpectedly raised the results again illustrated the greater reliability of the biochemical tests, especially if the criteria were made more stringent by insisting that two or more results must be abnormal before they were considered significant.

Table IV shows an analysis of the results obtained in 26 of the patients with clinically active rheumatoid arthritis who had a normal E.S.R. when tested on 38 occasions. It will be seen that individually the newer tests were by no means

* To some extent the unusually high figure of 30% is an artificial one, since patients showing this anomaly were specifically referred by colleagues for further testing.

TABLE III

RELATIVE RELIABILITY OF E.S.R. AND OTHER TESTS

Disease	No. of Cases Studied	Normal E.S.R.		Normal Index	
		No. of Cases	%	No. of Cases	%
Active rheumatoid arthritis ..	91	27	30	3	3·5
Active ankylosing spondylitis ..	14	1	7	0	0

Disease	No. of Cases Studied	Raised E.S.R.		Single Raised Index		Raised Index on Two or More Occasions	
		No. of Cases	%	No. of Cases	%	No. of Cases	%
Osteoarthritis ..	18	3	16·5	1	5·5	1	5·5
Non-articular rheumatism ..	8	3	37·5	3	37·5	1	12·5
Normal controls ..	53	4	8·0	5	10·0	1	0·5

TABLE IV

ANALYSIS OF 26 CASES OF CLINICALLY ACTIVE RHEUMATOID ARTHRITIS WITH NORMAL E.S.R.

Clinical Activity	No. of Cases	No. of Times Tested	Positive Reactions			
			T.P.P.	P:P	M.P.	C.R.P.
Grade 1	9	10	5	3	5	3
Grade 2	14	22	6	8	10	7
Grade 3	3	6	2	1	5	2
Total	26	38	13	12	20	12

as reliable in this group as they were collectively. By far the most consistent was the Winzler mucoprotein test, which showed raised levels in 50%, 45%, and 83% of the three grades respectively.

(2) PATIENTS WITH OBSCURE DIAGNOSES

Table V presents an analysis of 73 of the group of problem patients who were undiagnosable on the occasion of their first visit, but in whom incipient systemic disease was suspected. All these patients, on whom a total of 107

tests were made, were followed up for one year by means of personal interviews, but the second-year review had to be carried out largely from their hospital notes. They are classified according to the eventual diagnosis.

The Table illustrates clearly that in the group of patients who eventually turned out to have rheumatoid arthritis or one of the other collagenoses the new tests were significantly less reliable (69% error) than the E.S.R. (45% error), while the balance of advantage for the biochemical tests in the other group was not very startling (13·4% compared with 22% error).

TABLE V

TWO-YEAR FOLLOW-UP OF 73 "PROBLEM CASES" TESTED ON 107 OCCASIONS

Disease	No. of Cases	%	% Error in E.S.R.	% Error in Indices
Rheumatoid arthritis or one of its variants ..	35	48	45	69
Osteoarthritis; non-articular rheumatism; psychogenic rheumatism	38	52	22	13·4

The percentage errors in both groups analysed according to the individual tests are: E.S.R. 36·5; M.P. 36·5; C.R.P. 37·3; P:P 41·0; T.P.P. 46·7. Whereas the Winzler mucoprotein was again the most reliable of the newer tests, in no case was the error less than that for the E.S.R.

Table VI gives a detailed analysis of the tests carried out on patients with established rheumatoid arthritis classified into one of the five grades of activity

TABLE VI

ANALYSIS OF RESULTS ACCORDING TO GRADE OF ACTIVITY OF DISEASE

Grade of Activity	No. of Cases	Average Values				
		E.S.R. (mm. in 1 hour)	C.R.P. (units)	T.P.P. (mg. per 100 ml.)	M.P. (mg. per 100 ml.)	P : P
0 (inactive).. ..	10	10	0	167	17·8	2·41
1 (doubtful) ..	24	18	1	166	17·3	2·29
2 (mild)	59	26	1½	189	22·4	2·59
3 (moderate) ..	28	38	2	209	26·6	2·81
4 (fulminating) ..	4	77	4	228	36·7	3·37
	Total 125	Average for all Groups 28	1½	188	22·4	2·59

on each occasion the blood was drawn. The average values for each of the tests plainly illustrate that they reflect varying degrees of disease activity in *established* disease with commendable accuracy. It is impossible, however, to demonstrate any clear advantage for the newer tests over the traditional Westergren E.S.R.

DISCUSSION

The blood protein-bound polysaccharides and mucoproteins have been the subject of intensive study in recent years, and, whilst the startling headline* which recently appeared in an American newspaper may be dismissed as premature, it seems possible that with further refinements of technique their estimation may become indispensable to clinicians in the future. Since a rise or fall in the blood levels of these substances can occur in so many conditions, both physiological and pathological, they can so far be used only as non-specific indicators of disease processes; but if instead of measuring the *total* levels the carbohydrate moiety of each of the individual protein components of the serum was measured, it might be possible to characterize their *relative* levels as typical of different disease processes. This has been done in the case of rheumatoid arthritis by Kuhns and Crittenden (1955) with an electrophoretic technique. Shetlar and his colleagues (1949) compared the relative levels in cancer and arthritis, using a chemical precipitation technique to separate the protein fractions. It would appear that the same differential technique has now been applied with very interesting results to the three components of which the mucoproteins are formed (Price *et al.*, 1958).

Greenspan (1954) analysed the mucoprotein levels in 1,553 adult patients selected as being a representative cross-section of a general medical service. From his results he classified into broad groups the conditions which are respectively associated with raised and with reduced mucoprotein levels. He concluded from these and other observations that the blood mucoprotein level at any one time represented an equilibrium between certain hepatic and endocrine functions which when impaired tend to lower this level, and tissue proliferative and degenerative processes which when accelerated by any cause tend to raise it. Kelly *et al.* (1952) confirmed this and in addition postulated that stress phenomena acting via the pituitary–adrenal axis are accurately reflected by the mucoprotein level.

Shetlar and his colleagues in Oklahoma have investigated the serum protein-bound polysaccharides under a large number of conditions. For example, they (1949) found elevated levels in dogs in which sterile or bacterial

* "Blood Study Seen Quick Way to Diagnose All Disease. Medical Break Through?" (*Baltimore News Post*, March 19, 1958).

abscesses or talc granulomata had been created experimentally. Shetlar *et al.* (1955) also compared the total protein-bound polysaccharides, the mucoproteins, and the C-reactive protein in pregnancy, cancer, arthritis, and tuberculosis, with very interesting results. In 1953 they published a study of the levels found in degenerative arthritis compared with those in rheumatoid arthritis and other collagen diseases, with results which were sufficiently clear-cut to have encouraged us to proceed with the present investigation. However, unlike us, they found a striking lack of correlation between the polysaccharide percentage of serum protein and the E.S.R. in cases of established rheumatoid arthritis. In 1954 the same group of workers concluded that the best indication of rheumatoid activity was the ratio of the protein-bound polysaccharides to the total proteins (P : P), which ranged in their hands between 1·76 in normal controls and 2·96 in patients with active rheumatoid disease.

In 1955 Payne *et al.* used the P:P as a measure of the efficacy of phenylbutazone and cortisone in the treatment of rheumatoid arthritis. Both these drugs produced a significant fall in the P:P, and from this it was concluded that phenylbutazone had an anti-inflammatory rather than merely an analgesic effect in rheumatoid arthritis.

Kushner *et al.* (1956) carried out an intensive study of the serum mucoproteins both in patients and in healthy subjects. They found marked diurnal variations in the levels, suggesting that the serum should always be drawn at the same time of day. They also found that surgery caused a biphasic elevation, due first to the adrenal stimulation, and secondly to the tissue injury. It was suggested that the rise resulting from adrenal stimulation might invalidate the mucoprotein estimation as a test of disease activity in patients undergoing treatment with corticotrophin.

To explain these glycoprotein anomalies in inflammatory diseases Larsen and Hansen (1957) postulated a modification of protein synthesis resulting from the connective-tissue inflammation. In order to demonstrate this they measured the total sulphydryl concentration in ten patients with rheumatoid arthritis who were known to have increased polysaccharides and found that the blood levels of these substances bore an inverse relationship to each other. Furthermore, the depressed sulphydryl concentration tended to return to normal in five patients who were treated with corticotrophin.

The determination of C-reactive protein is by far the most sensitive measure of non-specific inflammation; in fact it may be considered too sensitive for routine purposes: for example, Yaffe (1957) found this test to be positive even with minor dental infection. However, it has one definite advantage—namely, that its level is not artificially depressed by steroids (Lewis *et al.*, 1957; Stollerman *et al.*, 1954), and therefore in patients undergoing treatment with these

drugs fluctuations in C-reactive protein level should reflect variations in disease activity more accurately than some of the other "acute-phase" reactions.

SUMMARY

A group of "acute-phase" reactions which have been commended by other workers have been evaluated clinically.

It is concluded that in established disease these new tests give fewer false negative readings than the erythrocyte sedimentation rate (E.S.R.). They are also slightly more reliable in relation to false positive reactions in "non-systemic" rheumatic disease. As a measure of disease activity in cases not receiving drugs they are approximately as accurate as the E.S.R. Of the individual tests, the Winzler mucoprotein test is slightly more reliable than the others.

However, in established disease the clinician does not often require laboratory help, and unfortunately in the group of "diagnostic dilemmas" where help is needed most these tests were disappointingly unreliable. Therefore there seems to be no justification for recommending that such time-consuming procedures should be added to the work of already overburdened laboratories serving rheumatism clinics.

The implications of some of the recent research work on serum glycoproteins and C-reactive proteins are discussed.

ACKNOWLEDGMENT

This study was carried out whilst working at the London Hospital under the auspices of Dr. W. S. Tegner, to whom we are grateful both for the facilities to carry it out and for permission to publish this report.

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CORRECTION

NOVEMBER, 1958, ISSUE

In Table II (p. 290) of the paper on "The Effect of Corticosteroids on the Skin Response to Ultraviolet Light in Rheumatoid Arthritis", by S. K. Banerjee and R. Harris, results are wrongly given as consistently E.1 against Week <1 for Subjects 3-8 and against Week 2-3 for Subjects 1-7. These lines should actually all have been blank, no tests having been made during these weeks on the subjects referred to.

ORIGINAL PAPER

THE USE OF EPOXY RESINS IN SPLINT-MAKING

By H. J. GLANVILLE

From the Rehabilitation Centre, Odstock Hospital, Salisbury

THE value of correct splintage is well recognized, but under hospital conditions it is often very difficult to provide adequate splints at short notice. Each case poses a separate problem, and calls for accurate fitting and often for the application of kinetic principles.

In our experience none of the methods and materials at present in vogue has been completely satisfactory. Most of the difficulties are due to the limitations imposed by materials. An ideal material for splint-making should: (1) be capable of direct moulding; (2) be strong, light, waterproof, chemically inert, and washable; (3) bond firmly to metal; (4) be such that it can be worked without special skill or apparatus; and (5) enable splints to be ready within a few hours of their prescription.

A review of the available materials suggested a trial of epoxy resin, and Messrs. Aero Research Ltd., of Duxford, kindly supplied samples of Araldite epoxy resins for this purpose. These are condensation products of epichlorhydrin and diphenylolpropane. A pigmented epoxy resin, "resin LW.2", was found to be suitable. It is supplied as a viscous paste, and cures after being mixed with "hardener 951" (triethylene tetramine), a liquid of low viscosity. For our particular purpose 100 parts by weight of LW.2 are mixed with 10 parts by weight of hardener and 30 parts by weight of "filler W", which consists of a combination of inert fillers such as marble flour. Curing takes place in fifteen hours at room temperature and in half an hour at 100° C.

METHOD EMPLOYED FOR SPLINT-MAKING

1. The thinnest possible cast is made from plaster-of-Paris bandage and applied direct to the part to be splinted. Three thicknesses of bandage are usually enough to hold the shape. When the cast is drying, loose plaster is removed with a dry nail-brush.

2. After the hardener, resin, and filler have been mixed the cast is thoroughly impregnated with mixture, using a stiff paint-brush. One or two layers of glass fibre, previously cut to shape and impregnated with resin, are then applied on the outer side to give strength, and such metal fixtures as may be required are slotted in between the layers of glass fibre and are held, if necessary, with a cotton stitch during setting.

3. The whole splint is placed in a domestic oven at 100° C. for the recommended time.

PLATE I

FIG. 1.—Self-retaining opposition splint.

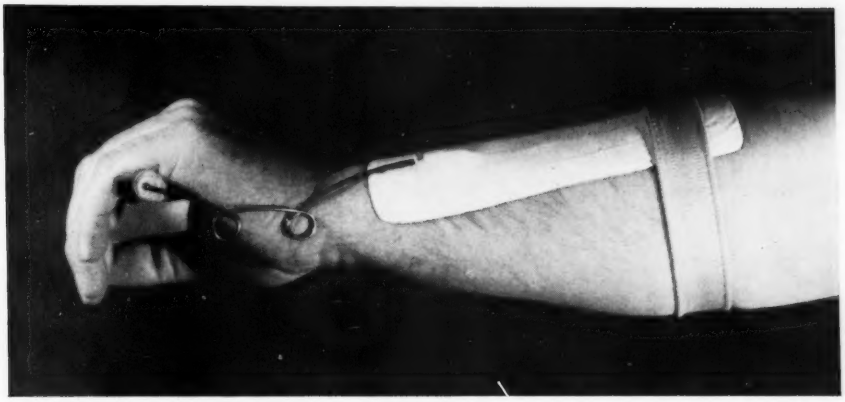

FIG. 2.—Ordinary radial palsy splint, the spring being held in two small tubes bonded into the material.

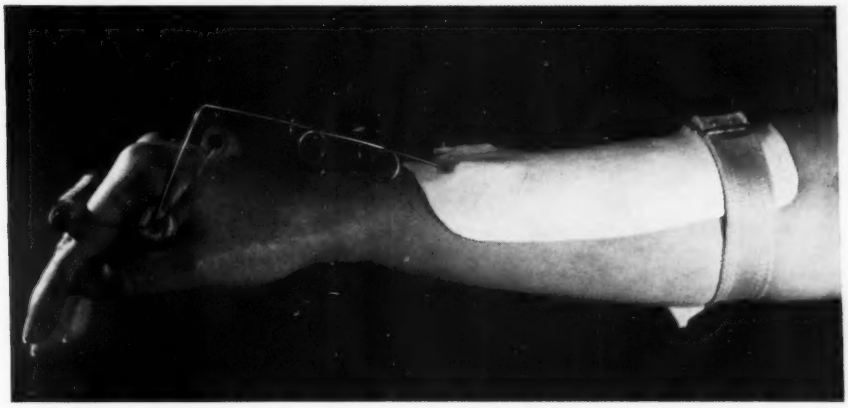

FIG. 3.—Same type of splint as Fig. 2 incorporating a knuckle-duster splint and suitable for a radial and ulnar lesion.

H.J.G. facing page 10]

4. After curing, the splint is cleaned and the shape adjusted, if necessary, with a file or sandpaper to obtain a perfect fit.

By this technique it is possible to obtain great versatility of shape, strength, and mechanical advantage, and the clinician is himself able to translate his prescription into material. The results have been encouraging, and it would seem that with this method some of the more complicated splintage problems could be brought within the scope of the general hospital.

Examples of splints made with resin are illustrated in Plate I.

PRECAUTIONS

The risks to operators using epoxy resins of contracting contact dermatitis or becoming sensitized have been pointed out in the literature. The dangerous ingredient is the hardener, triethylene tetramine. The following precautions have proved effective in our experience:

1. The operator should wear rubber gloves while working with the materials in the fluid state.
2. Care should be taken not to add an excess of hardener.
3. The ingredients should be thoroughly mixed to avoid local concentrations of hardener.
4. The splints should not be supplied to the patient until three or four hours have elapsed after baking.
5. Patients should be warned to report skin soreness and a search should be made for it at routine follow-up.

It is understood from the manufacturer that no case of dermatitis has been reported from contact with the *cured* resin during its industrial use, which has included such applications as coating finishes for food containers. During the last two years about 150 splints have been made by the technique described, and no case of dermatitis or sensitization has occurred. It would thus seem that the greatest potential danger is to the operator.

Acknowledgments

My thanks are due to the Director and staff of the Plastic Surgery Centre at Odstock for referring most of the patients; to Colonel E. Maltby for the original suggestion to carry out the research; to Dr. J. T. Scales, of the Department of Biomechanics and Surgical Materials, Institute of Orthopaedics; to Mr. Donald Perkins, of Kelvin Hughes Ltd.; and to my own staff.

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REVISION SERIES

PSORIASIS AND ARTHRITIS*

I—C. D. CALNAN

Royal Free Hospital, London

IT is heartening for dermatologists to feel that there now appears to be increasing agreement with their long-standing belief that there is a connexion between psoriasis and arthritis. But there are physicians who are still of opinion that the connexion between the two is no more than the coincidence of two common diseases.

This problem has been studied many times and discussed extensively in the medical literature. One of the most recent studies concerns a series of 293 patients with rheumatoid arthritis at the Massachusetts General Hospital (Short *et al.*, 1957). These authors list the following possibilities:

(1) So-called psoriatic arthritis is an independent entity resembling, but not part of, either psoriasis or rheumatoid arthritis.

(2) Psoriasis and rheumatoid arthritis share a common but unknown causation.

(3) The arthritis accompanying psoriasis is secondary to the skin disease, and may properly be labelled an arthropathy rather than an arthritis.

(4) The skin lesions constitute a manifestation of rheumatoid arthritis and may be called psoriasiform rather than true psoriasis.

(5) There is a constitutional, perhaps hereditary, tendency in certain individuals and families for the acquirement of both diseases, resulting in more frequent coincidence than can be due to chance alone. In certain of such cases the typical picture of the one disease may be modified by the presence of the other.

THREE BROAD ASSOCIATIONS

There is not a great deal of reliable statistical evidence from dermatological sources. The enormous variation in the manifestations and natural history of psoriasis forms an almost insurmountable barrier to accuracy in any statistical analysis. In general, we recognize three broad associations between psoriasis and rheumatism:

(1) *Non-articular Rheumatism.*—This group usually comprises patients who answer "Yes" to the general question, "Do you suffer from rheumatism or arthritis?" without showing recognizable signs of joint disease. This is the

* A symposium presented at a meeting of the Section of Physical Medicine of the Royal Society of Medicine, April 9, 1958.

largest group, and there is considerable difference of opinion as to whether such symptoms have any significance or not.

(2) *Rheumatoid Arthritis.*—In most of these cases there is little in the nature or behaviour of the arthritis to suggest that the association with psoriasis is more than coincidental. A few patients show a regular alternation of the two disorders, while others have exacerbations and remissions of both together. The onset of either may precede the other by many years, although it is usual for the psoriasis to manifest itself earlier. The recent observations of Wright (1956, 1957) on the Rose–Waaler differential agglutination test in this group are particularly interesting. His findings have been confirmed by Hess (personal communication, 1958), who has suggested that the presence of psoriasis in some way modifies the rheumatoid arthritis picture—the fifth possibility mentioned by Short *et al.* (1957) quoted above.

(3) *Psoriatic Arthropathy.*—This is the smallest group. Its most characteristic feature is the peculiar involvement of the terminal interphalangeal joint. Not infrequently also the psoriatic lesions in this group are atypical, and may not be recognized as psoriasis for many years. One such atypical variant is Reiter's syndrome; there are on record a number of cases of this syndrome whose subsequent course reveals that they are unequivocal psoriatics. Another variant is an abacterial inflammatory and pustular eruption of the hands and feet, especially on the finger tips and around the nails. This may be labelled acrodermatitis continua of Hallopeau or acrodermatitis pustulosa perstans of Sachs, as well as several other terms. Some of the patients are particularly striking, because the arthritic changes may be virtually confined to the digit or digits affected, and the nail dystrophy likewise.

NATURE OF THE PATHOLOGICAL PROCESSES

The precise cause of psoriasis is unknown. In spite of a number of claims for a specific infective agent (Benedek, 1955), it is doubtful if there is an identifiable single cause. Psoriasis would appear to arise as a result of three interacting factors. On a genetic background there is a biochemical disorder in the skin, which can be fired off by a number of triggers.

The Genetic Factor

The genetic basis is probably the most important part of the triad, and it has been studied extensively by many dermatologists and geneticists. The principal difficulties they have encountered are: (1) The first attack of psoriasis may occur at any age from infancy up to the ninth decade of life, and children may be affected before their parents. (2) Psoriasis may develop without the

victim being aware of it; for example, scalp lesions may be regarded as a normal amount of scurf, or nail involvement as being a variant of normality, or flexural lesions as a sweat rash. Hence every relative must be questioned and examined personally. But even then a person may develop the first lesions at any time after being examined and fail to report it. (3) While typical psoriasis is so characteristic that every practitioner can recognize it at a glance, there are many variants where even dermatologists cannot agree on the diagnosis. Some of these may start as what is apparently another disorder, but in the fullness of time become evident psoriasis. Examples of this are Reiter's disease, keratodermia climactericum, acrodermatitis continua, Leiner's disease, pustular bacteride, keratodermia blennorrhagica, erythrodermia, and acrodermatitis perstans. In fact, dermatological literature is strewn with descriptions of the odd and unusual manifestations of psoriasis.

In spite of these difficulties ample evidence has accumulated that psoriasis is inherited as a dominant with incomplete penetration. Estimates of the incidence of a family history in psoriasis vary from less than 1% up to 80%. Hoede (1957) found that the percentage rises with the length of history and that in patients with psoriasis of more than 30 years' duration it reaches 80%. A not infrequent pattern is to see only one person affected in each of three or four generations.

Disordered Physiology of the Skin

The problem of the disordered physiology of the epidermis responsible for the skin lesions seemed insuperable until recently. The chief function of the normal epidermis is to produce keratin and other substances to form a continuous stratum corneum. Psoriasis is characterized by an abnormal horny layer. For many years biochemical studies were concerned with changes in the general body metabolism of proteins, carbohydrates, choline, cholesterol, lipids, uric acid, and so on. These studies gave the same indecisive and conflicting results that ensued from the treatment of psoriasis with low-fat, low-cholesterol, high-sulphur, and many other dietary regimens. Apart from the arthritis under discussion, psoriatics are remarkably free from associated systemic disorders, and because of this some doctors tell their patients that psoriasis can be regarded as a sign of good health—a statement which does not always produce the consolation intended. It is remarkable how few patients see any connexion between their psoriasis and arthritis.

In recent years, however, notably in the United States, skin metabolism, especially the process of keratinization, has been studied extensively. In normal skin the stratum corneum consists of an insoluble fibrous protein, keratin, and a residue of other substances which total as much as 10 to 20% and comprise

amino-acids, polypeptides, and lipids. Some of them are extractable with fat solvents, and others with water. They are not wasted by-products, but have the important function of holding water in the horny layer. Normal shedding of the stratum corneum occurs in the form of invisible flakes of single or a few cells. The histological abnormality seen in psoriasis is the presence of nuclei still in the stratum corneum cells, and these cells do not separate into invisible flakes. Flesch and Jackson Esoda (1957a) have shown that this is associated with a physical and chemical abnormality in the non-keratin fraction of the horny layer.

The physical change is shown by extracting with a fat solvent and then measuring the time required for an oily liquid (e.g. squalene) to percolate through a column of the packed pulverized scales. The time values for psoriasis are many times greater than those for normal skin or other scaly dermatoses. The chemical differences which have been identified in the soluble fraction of the stratum corneum are a high sulphydryl and low free amino-nitrogen content. The insoluble keratin fraction is not abnormal in psoriasis. The sulphydryl changes can be seen histochemically (Flesch and Jackson Esoda, 1957b), and there are simple ninhydrin or chromatographic methods (Flesch and Jackson Esoda, 1957c) for the determination of free amino-nitrogen levels. The changes are believed to be specific and can be used as a diagnostic test. The same authors have suggested that this defective protein metabolism in psoriasis is dependent on an enzyme defect—a dipeptidase which is lacking an activator, rather than being inhibited. It is interesting that inorganic arsenic, which so consistently controls psoriasis, abolishes the sulphydryl content of the scales. It may be asked why this biochemical abnormality is usually exhibited only in discrete patches, is reversible, and recurrent at irregular intervals. There is no answer at present, but the same pattern of behaviour is seen in many other biochemical disorders, such as porphyria, sickle-cell anaemia, acholuric jaundice, and gout.

Trigger Mechanisms

Some trigger factor is evidently necessary to precipitate attacks of the disease. The diagnosis of trigger factors in diseases is nearly always based on circumstantial evidence only, and hence without proof; in the case of psoriasis there are four widely accepted trigger mechanisms: (1) streptococcal throat infections; (2) psychic trauma and stress; (3) physical trauma to the skin (Köbner phenomenon); and (4) sexual epochs. However, these factors do not automatically produce the disease in a genetically predisposed person; there must be inhibitors or "safety-catch" mechanisms present, and, to carry the analogy farther, one can say that in most instances removal of the trigger

pressure does not have any immediate effect in stopping the process "after the gun has been fired".

The Arthritis Component

There does not at first sight appear to be much connexion between this aetiological pattern and that of the associated arthritis. A genetic factor in rheumatoid arthritis is not prominent, although it can be found by careful search. Short *et al.* (1952) report a family history in 11·9% of patients and 5·1% of controls. Comparable figures given by Stecher *et al.* (1952) are 5% and 0·1%. A few families are recorded with four generations affected, and there is additional evidence from the study of twins.

As regards the biochemical disorder, more attention has been given to changes in polysaccharides than to the proteins of the connective tissue concerned, but there is evidence that there are physicochemical and chemical changes in the protein molecular structure in arthritis. Ziff (1952) found that the dilute-alkali-extractable material from rheumatoid arthritis lesions contained no hydroxyproline, but had an increased tyrosine and polysaccharide content.

Trigger factors in arthritis seem less distinct than in psoriasis, especially when subjected to statistical scrutiny, and there are the same difficulties with assessing circumstantial evidence.

To summarize, it can be said that a great deal of evidence has been accumulated in favour of a definite relationship between psoriasis and arthritis. The most likely explanation for this is that there is a constitutional tendency in certain persons to develop both diseases, and that one manifestation may modify the other; but on the evidence the verdict is "not proven".

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THE first mention of the association of psoriasis and arthritis seems to have been by Alibert in 1822 in a thesis on various aspects of psoriasis. Attention was focused more closely on the association by Bourdillon in 1888. Since then there have been numerous case reports and a few surveys, with conflicting opinions on the significance of the condition. In recent years workers with the Rose-Waaler differential agglutination test (D.A.T.) have found that most patients who had psoriasis with atrophic arthritis gave a negative D.A.T. (Ball, 1952; de Forest *et al.*, 1956; Jacobson *et al.*, 1956; Wright, 1957; Ziff, 1957). It was this observation that first stimulated the present re-investigation of the subject, and the following conclusions are based on a study of 154 patients with psoriasis and various rheumatic complaints.

CLASSIFICATION

Table I shows the composition of the series. In the patients who did not have erosive arthritis there were no unusual features of the skin or joint condition and their association seemed fortuitous. There were 118 patients with erosive arthritis, of whom 41 were men and 77 women. Clinically they fall into

TABLE I

COMPOSITION OF SERIES

Diagnosis	Males	Females	Total
Erosive arthritis	41	77	118
Osteoarthritis	9	14	23
Gout	2	0	2
Rheumatic fever	2	0	2
Muscular rheumatism ..	5	4	9
Total	59	95	154

three groups (Table II): (1) those with distal interphalangeal joint involvement; (2) those with a severe deforming arthritis; and (3) those whose condition was indistinguishable from rheumatoid arthritis.

1. TYPICAL DISTAL INTERPHALANGEAL JOINT INVOLVEMENT

There were 22 patients in this group, 10 men and 12 women. They showed the classical "psoriatic arthropathy" with distal joint involvement and nail

TABLE II

CLASSIFICATION OF PATIENTS WITH EROSIVE ARTHRITIS AND PSORIASIS

Type	Males	Females	Total
D.I.P.	10	12	22
Deformed	4	6	10
Indistinguishable:			
Positive D.A.T.	9	11	20
Negative D.A.T.	18	48	66
Total	41	77	118

changes of the same digits. In two patients the nails only were involved and the skin was clear. In eight patients there was a marked topographical association between nail and joint changes.

Plate II, Fig. 1, shows the contrast between an affected and unaffected nail with joint involvement. In this group the distal joints were commonly affected at the onset of the arthritis (Diagram 1), the joint involvement often

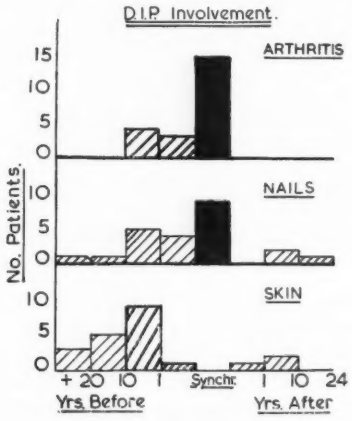


DIAGRAM 1.—Interval between diffuse interphalangeal joint involvement and onset of arthritis, skin rash, and nail changes.

being synchronous in onset with nail changes but never with the skin rash. In none of these patients was the arthritis limited to the terminal joints, and there seems no justification for restricting the term "psoriatic arthropathy" to those with arthritis affecting the terminal joints only (Bauer *et al.*, 1941). The arthritis was usually mild. The majority were little handicapped by it, and the functional

status at the time of examination was Grade 1 in 17 patients and Grade 2 in the other five. In all cases the D.A.T. was negative.

2. Severe Deforming Type of Arthritis

The second group of ten patients were severely deformed. Four had typical arthritis mutilans showing the classical opera-glass hand and a similar condition in the feet. All four had surprisingly little pain, and three had only moderate disability. The other six patients in the group showed severe deformity due to ankylosis and disorganization of many joints. Four were unable to walk, and the other two were very restricted in their activity. The greatest deformity possible in any form of arthritis occurred in these patients. The psoriasis was extensive and resistant to treatment in six of the ten. In every case the D.A.T. was negative. The sacro-iliac joints were involved radiographically in six.

3. Arthritis Indistinguishable from Rheumatoid Arthritis

The third group consisted of 86 patients with an arthritis clinically indistinguishable from uncomplicated rheumatoid arthritis. In 20 the D.A.T. was positive (that is, 23% of this group or 17% of the whole group), and it is thought they were examples of coincidental rheumatoid arthritis and psoriasis.

TABLE III

Functional Status of Patients with Psoriasis and an Arthritis Indistinguishable from Rheumatoid Arthritis

Functional Status	Negative D.A.T. %	Positive D.A.T. %
Grade 1	51	6
„ 2	24	35
„ 3	20	24
„ 4	5	29
„ 5	0	6
Total	100	100

Four had subcutaneous nodules—an incidence of 20%, which is the same as that in uncomplicated rheumatoid arthritis (Bennett, 1943; Wright, 1956).

In the 66 patients of this group with a negative D.A.T., the distribution of affected joints was similar to that in uncomplicated rheumatoid arthritis. The

arthritis was less severe than in uncomplicated rheumatoid arthritis or in the group with a positive D.A.T. Thus only 7·5% showed ulnar deviation, compared with 30% of those with a positive D.A.T. and 36% of an unselected group with uncomplicated rheumatoid arthritis. At the time of examination the functional status of the patients with a negative D.A.T. was better than that of those who gave a positive D.A.T. (Table III).

GENERAL FEATURES

In the group of patients with erosive arthritis 81% had nail changes. These were present in the fingers and toes in 57%, confined to the fingers in 11%, and to the toes in 13%. The changes included pitting (Plate II, Fig. 2), discoloration, hyperkeratosis (Plate II, Fig. 3), and ridging (Plate II, Fig. 4). In 310 patients with uncomplicated psoriasis nail changes only occurred in 18%.

A closer relation was found between nails and joints, both in the time of onset and the progress, than between skin and joints. A synchronous onset of nail and joint changes was commoner than of skin and joint changes (Diagram 2). It is of interest that the arthritis preceded the psoriasis in 27 patients by

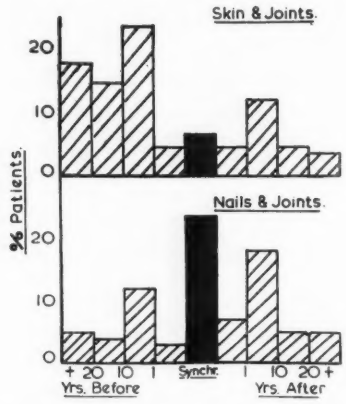


DIAGRAM 2.—Onset of arthritis related to onset of skin lesions and nail changes.

periods of up to 40 years. It is possible that some patients with erosive arthritis and a negative D.A.T. are destined to develop psoriasis.

The skin lesions were typical in site and character. Where the arthritis was severe, however, the psoriasis tended to be extensive and resistant to treatment.

There was a family history of psoriasis in 36% of these patients, whereas

PLATE II

FIG. 1.—Contrast between affected and unaffected nails with joint involvement.

FIG. 2.—Pitting of nails.

FIG. 3.—Hyperkeratosis of nails.

FIG. 4.—Ridging of nails.

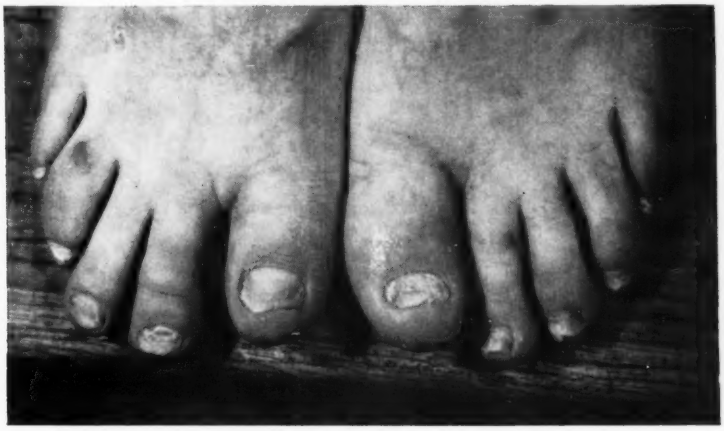
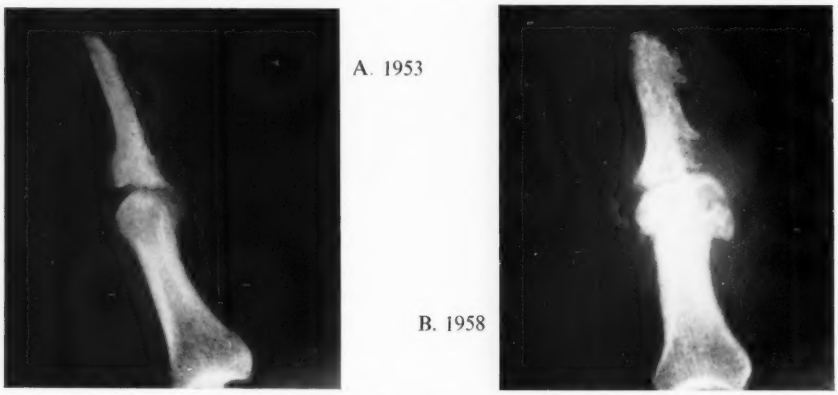


FIG. 5.—Case 3. Showing short big toes.

FIG. 1.—Case 3. Radiograph of right foot (1953) showing destructive changes at interphalangeal joint of big toe and terminal interphalangeal joints of 2nd and 4th digits. Early changes in two proximal interphalangeal joints. Note lack of osteoporosis.

FIG. 2.—Case 3. Lateral radiograph (1958) showing dorsal dislocation of distal phalanx of right big toe.

FIG. 3.—Case 5. Radiographs of feet (1958) showing almost complete destruction of distal phalanges of big toes.



A. 1953

B. 1958

FIG. 4.—Case 5. Radiographs of right thumb to show new bone formation.

[S.M. facing page 21

such a history was obtainable in only 3% of a group of patients with uncomplicated rheumatoid arthritis.

It has been stated by many authors that the arthritis clears up with adequate treatment of the skin lesions. In only six patients of the present series did that happen.

Radiographic features included distal interphalangeal joint involvement. The tips of the terminal phalanges as well as the distal joints were sometimes involved, and there was an increased incidence of sacro-iliac joint involvement.

ACKNOWLEDGMENTS

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III—STEPHEN MATTINGLY

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IT is difficult at present to determine the relationship between psoriasis and chronic polyarthritis, since we know so little about the aetiology and pathogenesis of these diseases. Moreover, the literature is confusing, partly because American physicians consider ankylosing spondylitis to be a variant of rheumatoid arthritis, and partly because the diagnosis of "psoriatic arthritis" has been claimed for different syndromes.

Some authors stress the close relationship between exacerbations and remissions of skin and joint disease, and the remarkable way in which complete

remissions may follow a severe and crippling attack of arthritis (Garrod and Evans, 1924; Nordin, 1934; Graham, 1935; Jeghers and Robinson, 1937). Others record the frequent involvement of the terminal interphalangeal joints, and in some patients these joints have been the only ones affected (Bauer *et al.*, 1941; Nunemaker and Hartman, 1950; Sherman, 1952; Sterne and Schneider, 1953; Wright, 1957). Radiologists in particular have noted unusual destructive changes in the small joints of the hands and feet (Plenk, 1950; Sherman, 1952; Sterne and Schneider, 1953; Fawcitt, 1950; Meaney and Hays, 1957), and recently it has been claimed that the Rose–Waaler test is usually negative in patients with psoriasis and chronic polyarthritis (Wright, 1956).

REVIEW OF CASES

A small series of 20 patients has been reviewed, but it is emphasized that the figures given here have no statistical significance. Patients were selected either because they had been seen personally in the past or because they were currently attending the Middlesex Hospital and the Arthur Stanley Institute for Rheumatic Diseases. In all cases the diagnosis of psoriasis was made by a dermatologist. The cases are divided into three groups (see Table).

TABLE SHOWING ANALYSIS OF CASES OF PSORIASIS AND ARTHRITIS

Diagnosis	No. of Patients	Sex	Involvement of Terminal Interphalangeal Joints	Rose's Test Positive	X-ray Changes in Sacro-iliac Joints
"Psoriasis arthropathica"	5	Male	5	1	0
"Ankylosing spondylitis"	3	Male	2	1	3
"Rheumatoid arthritis"	7	Male	2	6	1
	5	Female	0	2	2
Total	20 (15 Males)		9	10	6

(1) In the first group are five patients in whom the arthritis was largely confined to the terminal interphalangeal joints of fingers or toes; for convenience this condition is termed "psoriasis arthropathica". All five patients were men; in four Rose's test was negative; one patient had a positive Rose's test with a differential titre of 1 : 16, and he was the only patient in this group to give a history of a transient polyarthritis affecting other joints. None of

the five patients had a stiff spine or radiological changes in the sacro-iliac joints.

(2) The second group comprises three patients who appeared to have ankylosing spondylitis with peripheral joint involvement. All three were male, and in two the terminal interphalangeal joints were affected. The third patient was reported to have a positive Rose's test with a differential titre of 1 : 16. All three patients had a stiff spine, limited chest expansion, and fused sacro-iliac joints.

(3) In the third group were twelve patients who appeared to have rheumatoid arthritis. Six out of the seven men in this group had a positive Rose's test, and two of these had late involvement of terminal interphalangeal joints. Two of the five women had a positive Rose's test. Three patients were found on radiography to have minimal changes in the sacro-iliac joints compatible with the diagnosis of rheumatoid arthritis. None had a stiff spine.

Bauer *et al.* (1941) suggest that most psoriatic patients have rheumatoid arthritis (or rheumatoid spondylitis), and that if the term "psoriatic arthritis" were used it should be restricted to those cases in which the arthritis was limited to the terminal interphalangeal joints. The first group of cases in the present series therefore will bear more detailed discussion.

DETAILS OF CASES

Case 1

A man now aged 55 fell and stubbed the left ring finger in June, 1957. The terminal interphalangeal joint of this finger became painful and swollen, and after a few days he could no longer drive his car. The nail turned black, and was removed surgically four months later, but it failed to grow normally. Meanwhile patches of psoriasis developed on scalp, trunk, and legs, although he stated that he had no psoriasis before the accident, and he had no family history of psoriasis. In July, 1957, the right middle finger nail was affected by psoriasis, and a month later he noticed swelling of the terminal interphalangeal joint of this finger. The erythrocyte sedimentation rate (E.S.R.) and serum uric acid level were within normal limits and Rose's test was negative (1 : 8). Radiographs showed a marginal erosion of the distal phalanx of the left ring finger and some soft-tissue swelling, but no loss of joint space.

Case 2

An engineer aged 42 had developed psoriasis at the age of 16, and the nails were severely affected four years later. At the age of 34 he first experienced transient acute attacks of pain in, and swelling of, the terminal interphalangeal joints of the fingers, especially in the left hand. At first these attacks lasted only a few days, but swelling had persisted for the last two years and the joints hurt when gripping. His general health was good and no other joints had been affected. The psoriasis had never been severe and was mainly confined to the nails. One cousin, about the same age, had a similar complaint.

The E.S.R. and serum uric acid level were within normal limits and Rose's test was negative. Radiographs of chest, sacro-iliac joints, and feet were normal; radiographs of the hands showed soft-tissue swelling of most of the terminal interphalangeal joints, with expansion of the base of the distal phalanx and marginal erosions; there was little, if any, osteoporosis and the joint spaces were well preserved.

The patient has received a three months' course of gold injections without benefit, and recent superficial radiotherapy, to the nails only, has been without effect.

Case 3

A watch repairer aged 46 developed psoriasis at the age of 18, and his nails were probably affected some years later. At the age of 25 he stubbed the right big toe and it had ached since, with occasional acute attacks of pain lasting several days, usually following some minor trauma. At the age of 38 the terminal interphalangeal joints of the left thumb, index and ring fingers became swollen and painful, and this arthritis seemed to be related to the condition of the appropriate nail.

When first seen in 1953, at the age of 40, he complained of pain in the fingers of the left hand, both thumbs, and both big toes. The skin on the dorsum of fingers and toes was red, warm, and moist, and all the nails were severely affected by psoriasis. Both big toes were short and swollen (Plate II, Fig. 5), but the right big toe was more deformed than the left, and a chronic paronychia was present. He stated that he frequently expressed pus from under this nail fold, especially after a hot bath; this "pus" was cultured and grew a pure culture of *Staphylococcus albus*. The right big toe was extremely mobile on passive movement. No other joints were affected and the spine was mobile. There was no neurological disease. His sister had psoriasis, and his father had had psoriasis and ? gout.

The patient's E.S.R., serum uric acid, and serum cholesterol were within normal limits, and the blood Wassermann, Kahn, and Rose's tests were negative. Radiographs of the hands in 1953 showed soft-tissue swelling of the affected joints with a few small marginal erosions, but no osteoporosis or loss of joint space. Radiographs of the feet (Plate III, Fig. 1) revealed marked destruction of the interphalangeal joint of the right big toe and of both phalanges, with expansion of the base of the distal phalanx and an erosion extending along the shaft of the proximal phalanx; there was no osteoporosis. Similar, but less marked, changes were seen in a few other distal interphalangeal joints and in one proximal interphalangeal joint in the right foot. Marginal erosions were also present in the interphalangeal joint of the left big toe.

Radiotherapy was given to the distal joints of hands and feet with marked relief of symptoms for five years, though pain was not relieved for several weeks following treatment. Radiographs in 1958 showed little change in the joints. A lateral radiograph of the right big toe showed that the distal phalanx had dislocated dorsally (Plate III, Fig. 2). Radiographs of sacro-iliac joints were normal.

Case 4

A salesman aged 51 had developed psoriasis at the age of 18, and his nails were affected a few years later. His right big toe began to ache when he was 36, but there had been no acute attacks of pain in the foot suggestive of gout. At the age of 48, after three years without active psoriasis, he woke one morning with painful swollen wrists. While the arthritis improved over the next few days, the psoriasis became

generalized and the skin of the hands, never previously affected, peeled off. Within a week the terminal interphalangeal joints of the fingers became red and swollen; the feet and ankles also swelled and became painful. The arthritis improved after a few weeks, but the patient was admitted to hospital three months later for treatment of the psoriasis.

When first seen at this time he had severe psoriasis of the trunk, hands, and feet. The distal interphalangeal joints were swollen and tender and there was marked shortening of the right big toe. A throat swab grew haemolytic streptococcus Group A and he was given a short course of penicillin. The psoriasis improved rapidly with bed rest and local applications, and, whilst the joints improved with rest and aspirin, pain persisted. The distal joints were therefore treated with radiotherapy, and he became free from pain after six weeks. He remained well and without joint symptoms for nearly three years, but has recently received further radiotherapy for pain in the feet and in the metacarpophalangeal joint of the right ring finger. No other joints have been affected and his spine has remained mobile. He still has generalized psoriasis, but no lesions on the hands or feet. There is no family history of psoriasis or arthritis.

The patient's blood Wassermann and Kahn tests were negative and the serum uric acid level within normal limits. The E.S.R. was 60 mm. in one hour (Westergren) during the acute polyarthritis, and a recent Rose's test was positive at a differential titre of 1 : 16. Radiographs in 1955 showed only soft-tissue swelling of the terminal interphalangeal joints of the fingers, but destructive changes were present in the interphalangeal joint of the right big toe and similar, but less marked, changes in the distal and proximal interphalangeal joints of the fourth right toe. Recent radiographs showed some increase in the size of erosions of these joints; soft-tissue swelling was no longer present in the fingers. Radiographs of chest and sacro-iliac joints were normal.

CASE 5

A clerk aged 41 had developed psoriasis at the age of 16 and his nails were probably affected by the age of 20. At 34 he started to experience acute attacks of pain in the right thumb and both big toes with redness and swelling of the joints. These had remained swollen, although he had had no acute attacks of pain for the last two years. The terminal interphalangeal joint of the right middle finger had been affected recently. There was marked shortening of the right thumb and both big toes with swelling of the interphalangeal joints. The E.S.R. and serum uric acid were within normal limits on several occasions, and Rose's test was negative. The patient was well, had a mobile spine, and no neurological disease.

Radiographs of the feet (Plate III, Fig. 3) showed almost complete destruction of the distal phalanges of the big toes, though the proximal phalanges were relatively normal. There were minimal changes in other distal interphalangeal joints similar to those seen in the previous cases. Radiographs of the hands showed soft-tissue swelling of the terminal interphalangeal joint of the right middle finger, with a ragged erosion on the anterior aspect of the distal phalanx; the joint space was well preserved. In 1953 the terminal phalanx of the right thumb appeared to have an erosion extending along the anterior surface of the shaft, but five years later the bone had re-formed, soft-tissue swelling was more marked, and there appeared to be ectopic bone dorsal to the interphalangeal joint (Plate III, Fig. 4).

DISCUSSION

These five patients appear to have an arthritis mainly confined to the distal joints of hands or feet, and four of them have now had their arthritis for 7, 8, 15, and 21 years respectively. All five patients have severe psoriasis of the nails, which seems more closely related to joint symptoms than does psoriasis of the skin. A topographical relationship between affected nail and joint has previously been noted in the literature (Dawson and Tyson, 1938; Nunemaker and Hartman, 1950; Sherman, 1952). Three patients with marked shortening of the big toes and resorption of the phalanges have had a chronic paronychia, and two could express "pus" from under the nail fold of the right big toe after a hot bath; it may be significant that these two patients benefited from radiotherapy and that the paronychia had disappeared three years later. Four of the patients had experienced acute attacks of joint pain suggestive of gout, but in no way typical of acute gout, and the serum uric acid level was never raised. Similar attacks have previously been described in the literature (Dawson and Tyson, 1938; Sherman, 1952; Wright, 1956). It should be emphasized that all five patients are well and little troubled by their joint disease, and this may account for the fact that similar cases are seldom seen in hospital clinics. No patient was found to have neurological disease or diabetes, and the blood Wassermann and Kahn tests have been negative. One patient, with a history of acute polyarthritis three years ago, is now reported to have a positive Rose's test (1 : 16).

The three patients in the second group of this series of 20 cases appear to have typical ankylosing spondylitis which responded well to radiotherapy, although Sharp (1957) has suggested that psoriatic patients have atypical spondylitis which is not benefited by radiotherapy. All three patients have peripheral joint involvement, and in two the terminal interphalangeal joints have been affected at a late stage of the disease. In one of these patients radiographs show unusual atrophy of the tufts of the terminal phalanges, and in the other case progressive changes in the terminal interphalangeal joints similar to those usually seen in the joints of the hand in severe rheumatoid arthritis. In both cases proximal interphalangeal joints have also been affected. Spondylitis has frequently been described in psoriatic patients (Dawson and Tyson, 1938; Bauer *et al.*, 1941; Sherman, 1952; Sterne and Schneider, 1953; Fletcher and Rose, 1955; Wright, 1956), but the literature is confusing because American physicians consider ankylosing spondylitis to be a variant of rheumatoid disease (Short *et al.*, 1957).

Patients in the third group appear to have rheumatoid arthritis, and Rose's test is positive in 8 out of the 12, including two patients with arthritis of the

terminal interphalangeal joints; in five the differential titre is at least 1 : 64. Sharp (1957) noted a positive Rose test in 11 out of 39 patients tested, although Wright (1956) found a positive result in only 2 out of 34 patients. These conflicting findings may be due to different laboratory techniques or selection of patients. Three patients in this group have minimal radiological changes in the sacro-iliac joints, but these are compatible with a diagnosis of rheumatoid arthritis. None of these three patients has a stiff spine.

Fifteen of the 20 patients in the series, therefore, have a chronic polyarthritis resembling rheumatoid arthritis or ankylosing spondylitis. Only two have noted coincident exacerbations of skin and joint disease, and no patient with normal nails has developed arthritis of terminal interphalangeal joints. The first five patients appear to have a different joint disease. Is this a specific psoriatic arthropathy?

The term "psoriatic arthritis" has been used to describe three different groups of patients: (1) Bauer *et al.* (1941) would confine its use to cases in which the arthritis is restricted to the terminal interphalangeal joints. In two of the cases here described other joints are, or have been, affected. (2) Sherman (1952) defined the condition as an arthritis, associated with psoriasis of the nails, which starts in the distal joints of hands and feet but may progress to involve other peripheral joints. She made a comprehensive pathological study of 15 cases. Biopsy revealed non-specific inflammation of the affected joints, but she noted absence of pannus and subchondral erosions, cartilage being destroyed from the periphery by marginal erosions which sometimes extended along the shaft of the phalanges. The end-result was destruction of bone and joint and their replacement by dense fibrous tissue, and sometimes ectopic bone was formed. Bauer *et al.* (1941) found similar changes in one patient whose arthritis was limited to the terminal interphalangeal joints for 44 years. Sherman's definition of "psoriatic arthritis" would cover the five cases here presented, and she describes a number of very similar cases. (3) Wright (1956) has recently suggested that most patients with psoriasis and arthritis have a negative Rose's test and a disease which can be distinguished from rheumatoid arthritis, while Sharp (1957) considers the spondylitis found in association with psoriasis to be atypical.

CONCLUSIONS

It seems probable that psoriasis and chronic polyarthritis occur together more frequently than can be explained by a chance association of common diseases. It is possible, but not proven, that some psoriatic patients with arthritis have a specific arthropathy. It is evident that, in any case, patients

with psoriasis of the nails tend to develop an arthritis of the related terminal interphalangeal joints, and in a few cases these are the only ones affected. The unusual radiological changes which are sometimes seen in such patients may result from the indolent nature of their disease, though the effect of trauma, of low-grade infection, or of vascular changes, perhaps associated with chronic paronychia, cannot be discounted. The response to radiotherapy of two patients in the present series is interesting, for Popp and Addington (1941) found that radiotherapy benefited eight out of nine patients whose nail psoriasis was associated with pain and swelling of the related terminal interphalangeal joint.

Acknowledgments

I am indebted to many colleagues for their help, in particular to Dr. A. C. Boyle, Dr. H. A. Burt, Dr. P. J. Hare, Dr. R. H. Meara, Dr. G. O. Storey, and the physicians attending the Arthur Stanley Institute for allowing me to see their patients. I am grateful to Mr. Turney and the staff of the Photographic Department of the Middlesex Hospital for the illustrations.

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BRITISH ASSOCIATION OF PHYSICAL MEDICINE

1958 PROVINCIAL MEETING

THE 1958 Provincial Meeting of the Association was held at the St. Andrew's Brine Baths and the Winter Gardens, Droitwich, on October 24 and 25, 1958, with the Vice-President, Dr. H. A. Burt (London), in the Chair.

After welcoming the members of the Association, Dr. J. W. T. PATTERSON (Droitwich) gave a vivid, though necessarily condensed, history of the place from pre-Roman times to the present day. His illustrations gave an excellent idea of both the medicinal and commercial aspects of the use of brine, and also of the processes involved all through the ages in converting it from its natural state to a form useful to man.

SCIENTIFIC PROCEEDINGS

ALKAPTONURIA

Dr. C. F. HAWKINS (Birmingham) presented an account of the detection and investigation of a case of alkaptonuria. In itself this had provided a great deal of interest, but the investigation of the family history in the field had also been fruitful. In telling his story Dr. Hawkins dealt with every aspect of this interesting disorder, but the climax was reached when he presented a photographic slide which had actually been developed in the patient's urine. (It is hoped to publish this paper in full at a later date.)

CURRENT TRENDS IN THE MANAGEMENT OF RHEUMATOID ARTHRITIS

Opening a discussion on current trends in the management of rheumatoid arthritis, Dr. BARBARA ANSELL (London) gave a panoramic review of the subject. She felt that salicylates, education, and physiotherapy remained the mainstay of treatment. Admission to hospital led to better assessment of a case than was otherwise possible, but bed rest became a grave risk if full services were not available to maintain proper posture and muscle function. The indications for steroid therapy were overwhelming disease or severe systemic manifestations such as arteritis. It was essential to appreciate the need for co-operation with the orthopaedic surgeon and with ancillary services, such as that provided by the occupational therapist. (Dr. Ansell's paper will be published in the Revision Series of the *Annals* in due course.)

In the ensuing discussion Dr. Ansell said that patients had experienced little gastro-intestinal trouble when taking doses of phenylbutazone of the order of 200–300 mg. per day. She agreed with Dr. Hawkins that, because of the risk involved, she would be unwilling to use this drug in combination with steroids by mouth. Dr. A. T. Richardson (London) felt that gastro-intestinal upset due to cortisone and similar drugs was more common in rheumatoid arthritics than in, say, dermatological cases treated with steroids, and he felt that there might perhaps be a particular hazard inherent in the combination of steroids with salicylates. In some areas in Great Britain great difficulty was still experienced in obtaining good physiotherapy, the importance of which had been indicated by Dr. Ansell.

Dr. D. Wilson (Chichester) agreed with Dr. Ansell concerning the importance of explaining to the patient the meaning of the disease, particular stress being placed upon the fact that a long-term view must be taken. He felt that efforts should be made to ensure that all doctors appreciated the danger of suddenly withdrawing steroid drugs. Referring to the question of amyloid disease which had been raised earlier by Dr. Ansell, Dr. Wilson said that he felt a number of cases would be missed if the diagnosis was to depend entirely on the finding of proteinuria. He had the impression that amyloid disease did badly when treated with steroids.

Dr. P. Kidd (Worcester) queried whether in fact these drugs actually precipitated the appearance of amyloidosis as a complication of rheumatoid disease. Dr. Ansell felt that amyloid disease was easily diagnosed on gum biopsy in the out-patient department. No hard-and-fast rules as to treatment could be laid down and each case must be considered on its merits. Some severe cases of rheumatoid arthritis had developed amyloid disease whilst on steroid therapy, and she felt that, although there was no positive evidence to suggest that steroids aggravated the disorder, they certainly did not prevent it. A great deal more experimental work was needed on the deposition of amyloid.

Replying to Dr. Hawkins, Dr. Ansell said that in pregnant women on steroid therapy spontaneous abortion at the second month appeared to be common. Congenital malformation of the foetus was also a possible risk. Although no steroid booster dose was necessary as a routine before labour, such was obviously indicated, in common with any operation on a patient taking steroids, before caesarean section. Emergency gastrectomy might be required occasionally in the treatment of haemorrhage or perforation arising as a complication of corticosteroid treatment, but elective gastrectomy was only very rarely indicated in patients with a history of severe gastric complications and in whom continued treatment with steroids was obligatory for the maintenance of life.

Dr. A. C. Boyle (London) said that Dr. Ansell had mentioned synovectomy in the treatment of the rheumatoid knee-joint, and he would like to know what she thought were the indications for this procedure, which was considered by many people to be thoroughly bad. In his experience pain and swelling recurred very quickly after synovectomy, and instability of the knee-joint seemed to occur frequently. Dr. Ansell agreed that instability could be a real problem, but it was one that could be minimized if the surgeon made every effort to avoid damage to ligaments. Some cases, reviewed up to ten years post-operatively, had done well. The indication for the operation was knee effusion which was severe enough to prevent the patient working and which was uncontrolled by injections of hydrocortisone repeated at three-week intervals or less. Good physiotherapy from the immediate post-operative period was essential.

Dr. H. A. Burt said that intrasynovial washout used to be very effective, but it was a method of treatment that seemed to have gone out of fashion. He agreed with Dr. Boyle that he had seen some bad results follow synovectomy. He had the impression that poor scar formation sometimes occurred as the result of steroid therapy, but Dr. Ansell felt that the skin of some rheumatoid patients tended to be difficult to heal quite apart from steroids.

In reply to Dr. P. Kendall (London) Dr. Ansell said that polyarteritis nodosa had been seen in conjunction with rheumatoid arthritis long before the advent of the

steroid preparations. The use of steroids had probably stimulated a search for the arteritic lesion because of an increased awareness of its existence.

Some speakers inquired whether gold and steroid therapy could be combined. Dr. Wilson stated that no added side-effects were encountered in these circumstances, and it was apparent that some rethinking was required on the whole question of chrysotherapy. Dr. Ansell reported that workers in Manchester were attempting to titrate disease activity against the effectiveness of gold, in some cases using doses of up to 200 mg. of gold three times a week.

Dr. J. Shulman (Coventry) remarked that he seemed to see more rheumatoid arthritis of late onset, in the seventh and eighth decades, than he used to do, and wondered whether this was an isolated impression. A number of members agreed that this was their common experience, and Dr. K. Lloyd (Cardiff) suggested that it was due to the fact not only that the milder cases were now recognized for what they were, but that general practitioners had also come to realize that something could be done to help them.

Discussion on the L.E. Cell

A discussion on the L.E. cell was opened by Dr. P. Kidd (Worcester) and Dr. J. M. Malins (Birmingham). Speaking on the laboratory aspects of the L.E. cell phenomenon, Dr. Kidd said that after the pioneer work of Hargraves and others using bone marrow many different techniques had been devised to demonstrate L.E. cells in peripheral blood. All methods had in common the need to provide for the interaction of active phagocytic leucocytes, L.E. serum factor, and nucleoprotein derived from disintegrating cells. The Snapper–Nathan technique, while capricious as a routine diagnostic method, could yield L.E. cells in large numbers. L.E. cells must be distinguished from tart cells—mononuclears or polymorphonuclears which had ingested intact lymphocyte nuclei. Erythrophages, degenerating nuclei or polymorphonuclears, and amyloid inclusions had occasionally caused confusion. The test was not positive in all cases of systemic lupus erythematosus (S.L.E.), and a combination of different tests might prove valuable.

Earlier work had suggested that the L.E. inclusion consisted of depolymerized desoxyribonucleic acid (D.N.A.). Recent histochemical work had shown, however, that L.E.-body transformation resulted in the gain of a protein foreign to the nucleus and displacement of histone from its linkage with D.N.A. Fluorescent antibody techniques showed that the L.E. factor combined with the nucleus of tissue cells, and, moreover, this antinuclear factor might be demonstrated in some conditions which gave negative reactions to conventional L.E. cell tests.

Dr. Malins described how the discovery of the L.E. cell in 1950 had revived Osler's concept of lupus erythematosus as a disease with widespread visceral lesions, sometimes with a chronic course. In a four-year period 337 L.E.-cell tests had been performed at the Birmingham General Hospital. Of 37 positive results, 9 had occurred in patients with typical subacute S.L.E. and 28 in cases of chronic rheumatoid arthritis. The latter appeared to have conventional joint lesions clinically. In 13 of these cases, although the disease had been present for an average duration of 12 years, there had never been any systemic manifestations. However, the appearance of systemic lesions might be delayed for 20 years or more from the onset of the arthritis. Renal involvement resulting in death in uraemia had occurred in two cases.

The finding of L.E. cells, though it presumably indicated the presence of an abnormal γ-globulin, did seem specific for this disease, at least if the simpler techniques, such as that of Magath and Winkles, were used. False positive results did not as a rule survive criticism, except for those reported in association with sensitivity to hydrallazine. Dr. Malins suggested that rheumatoid arthritis and S.L.E. were the results of one disease process, though perhaps differing in aetiology.

During the discussion which followed Dr. Ansell drew attention to the importance of the prognosis as a distinguishing feature between S.L.E. and rheumatoid disease: it was essential to distinguish between S.L.E. and rheumatoid arthritis with systemic manifestations. Dr. Richardson felt that the low incidence of erosive joint changes in S.L.E. as compared with rheumatoid arthritis was a useful diagnostic point. Dr. Malins thought that liver disease could be accepted as a manifestation of S.L.E., and Dr. Boyle agreed with him that the finding of the L.E. cell in an apparently uncomplicated case of rheumatoid arthritis suggested that other manifestations of S.L.E. would occur in due course.

Speakers expressed some disagreement as to the value of steroid drugs in preventing the onset of systemic manifestations of the disease, particularly the renal lesions. Dr. Malins felt that they might suppress the manifestations but probably did not alter the course of the disease. He personally had not had the courage to avoid giving steroids in these cases. Dr. Richardson said that renal lesions did in fact develop while patients were taking steroids, and he felt that the indications for the use of these preparations in S.L.E. were open to question, except when they were necessary to deal with lethal manifestations.

Rheumatism in Man and Beast

In a paper entitled "Do We Limp Alone?" Dr. J. E. Dawson (Droitwich) made an intriguing excursion into the field of comparative rheumatic pathology. The pathology of degenerative joint disease was known to have been essentially the same for some 100,000,000 years. Both fossils and contemporary animals exhibited most of the rheumatic conditions to which man was heir, and recently a great deal of research had been carried out on both domestic animals and wild animals in captivity. Hypertrophic joint disease and periarticular disease were more prominent in carnivora, while atrophic and erosive joint disease was seen more frequently in herbivorous animals. Even birds were subject to gout.

Demonstrations

An X-ray demonstration was given by Dr. Hawkins, and the remedial team gave a practical demonstration of various rehabilitation methods.

SOCIAL ACTIVITIES

Members never cease to be grateful for the excellent hospitality offered by their hosts at the provincial meetings of the Association, and the Vice-President had the unstinted support of all present when he thanked Dr. Patterson and his staff, the directors of the Spa, and all those others who had made this a memorably successful scientific and social gathering.

D. R. L. Newton

BOOK REVIEWS

PHYSIOTHERAPY IN CHEST DISEASES. By Torsten Bruce, Caroline Reutersward and Brigit Westin. *Pp. 97. 12s. 6d. London: National Association for the Prevention of Tuberculosis. 1958.*

This small book, first published in Sweden, is intended as a guide for physiotherapists in the management of thoracic surgical cases and disease of the lungs and pleura, with special emphasis on tuberculosis. The first section consists of a brief and simplified description of the various pathological conditions and the surgical procedures used in treatment. The section on physiotherapy has been written by two Swedish physiotherapists. The views expressed for the adoption of various postures to assist breathing are by no means accepted in Great Britain as of value in controlling movement of different parts of the diaphragm. Electrical stimulation of the diaphragm via the phrenic nerve in the neck is advocated where the diaphragm does not regain satisfactory mobility following pleural effusion.

In the section on postural drainage, not enough emphasis is placed on the importance of this form of therapy. The postures for draining the various segments and lobes described in the text would be clearer and of more practical value if diagrams of these positions had been included, together with an illustration of the anatomy of the bronchial tree. In order to gain the maximum aid of gravity a thorough knowledge of the bronchial tree is essential. No time or duration for tipping is stated.

The correction of postural deformities and of immobility of the shoulder following thoracic surgery is well presented.

JOYCE P. LOMAS

THE HANDICAPPED AND THEIR REHABILITATION. Edited by Harry A. Pattison. *Pp. 944. £5 12s. 6d. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications. 1957.*

Forty-four contributors have taken part in the production of this large book. All are American except one from the United Kingdom.

Part I consists largely of extracts from the writings of Kessler, Knudson, and Rusk concerning the need for dynamic restorative therapy for the handicapped. Although no historical section is supplied, there remains the impression that rehabilitation started during World War II, and the contribution of Sir Robert Jones, for example, in training American doctors at Shepherd's Bush in World War I is ignored. The role of the "Rehabilitation Counsellor, Co-ordinator or Executive Assistant" is stressed throughout the book. Part II is devoted to the rehabilitation of specific disabilities. The "Patient with Heart Disease" is particularly worthwhile. The section on "Plastic and Reconstructive Surgery" is very detailed and technical. Part III defines the roles of the members of the rehabilitation team. The contributions of the co-ordinator, medical social worker, nurse, occupational therapist, vocational counsellor, physical therapist, educational therapist, manual arts therapist, music therapist, psychologist, and the clergy are discussed fully. Part IV is concerned with such topics as fatigue, nutrition, home-bound employment, ergotherapy, placement and resettlement, and the interaction of the various agencies in this respect. It refers almost exclusively to American practice.

There is a tremendous amount of useful information stored in this book. The constant attention to the need for co-operation and the necessity for "individualization" in all procedures for handicapped persons is significant and could well be implemented more fully in Great Britain.The production is good, and the reproduction of the photographs superior to that of many American textbooks. I was unfortunate enough to receive a copy which had at least fifteen blank pages scattered through the text. The varying styles of the contributors make consecutive reading difficult, but as a reference book it should prove of value to personnel working in the field in the United States of America. Its value in Great Britain is obviously limited, but many of the techniques and some of the philosophy are worthy of careful consideration.

JAMES G. SOMMERVILLE

REHABILITATION AFTER ILLNESS AND ACCIDENT. Edited by T. M. Ling and C. J. S. O'Malley. *Pp. 119. 12s. 6d. London: Baillière, Tindall and Cox. 1958.*

There are eight contributors to this book, all of whom are associated, either as consultants or as past students, with St. Thomas's Hospital. It is a slim volume of some 120 pages, with ten chapters devoted to the psychological effects of sickness and injury, to the place of rehabilitation in the treatment of medical and surgical cases including such specialized problems as head injuries, and to the organization of rehabilitation in Great Britain. This last chapter could with advantage be expanded. An appendix lists industrial rehabilitation units and various training centres.

There has been an increased interest in rehabilitation and resettlement since World War II, and it is evident that this should be the concern of all doctors as well as of social workers, physiotherapists, occupational therapists, and officials of the Ministry of Labour. This book is intended for all workers interested in this field, and it is also hoped that it will prove of value to medical students and social workers in training. It contains a good deal of useful information and wisdom based on experience, but like many other books written by a panel of contributors there tends to be repetition. Despite this criticism I can recommend it to those interested in physical medicine, and especially to those taking the Diploma in Physical Medicine.

S. MATTINGLY

ABSTRACTS OF THE LITERATURE

Electrodiagnostic Stimulators. A Report by a Subcommittee of the Medical Research Council's Nerve Injury Committee. *Brit. med. J.*, 1958, **2**, 714.

This is the report of a subcommittee set up to advise the Ministry of Health on the best type of stimulator for routine clinical electrodiagnosis. The R.A.F. stimulator (Type V), having been proved to be an accurate and satisfactory voltage-calibrated apparatus, was carefully compared with the current-calibrated generator produced by Dr. P. Bauwens. The clinical trials were carried out at the R.A.F. Rehabilitation Centre, Chessington, St. Andrews University, and St. Thomas's Hospital. Both types of stimulator were found capable of providing the information required for assessing the extent of muscle denervation by means of intensity–duration curves. The subcommittee stresses that the most reliable indication of partially innervated states is the detection of discontinuities in the intensity–duration curves. Although the current-calibrated stimulator is theoretically and technically more accurate than the voltage-calibrated apparatus, for the practical purposes of diagnosis there is no real difference in accuracy. Patients in general prefer the constant-voltage stimulator, and indeed some would not tolerate the constant-current apparatus. Skin preparation is more important in the case of the voltage-calibrated apparatus, but alterations in skin resistance have no effect on the shape of the intensity–duration curves.

The report details the specifications of a voltage-calibrated generator which the subcommittee considers adequate for general use.

P. J. R. NICHOLS

Clinical Features and Course of Ankylosing Spondylitis. M. WILKINSON and E. G. L. BYWATERS. *Ann. rheum. Dis.*, 1958, **17**, 209.

This is an interesting review of over 200 cases of ankylosing spondylitis seen and followed up at Hammersmith Hospital, London, over a period of sixteen years. The authors believe that ankylosing spondylitis is a slowly progressive condition which does not remit completely or permanently, although iritis and new peripheral joint lesions are uncommon in the later stages of the disease. They found that radiotherapy often gave temporary relief, but this was short-lived in many cases. Despite prolonged illness, patients often remained at work, though they tended to select light occupations. The disease rarely shortened life. The authors were unable to distinguish subgroups on the basis of an association with rheumatic fever, psoriasis, or urethritis.

S. MATTINGLY

Arthritis Associated with Ulcerative Colitis. E. G. L. BYWATERS and B. M. ANSELL. *Ann. rheum. Dis.*, 1958, **17**, 169.

The authors review 37 cases of colitis in association with arthritis. They conclude that the arthritis in such cases usually differs from rheumatoid arthritis, tending to be mild, remitting, and often migratory. Only two patients had subcutaneous nodules and a positive D.A.T. In seven patients acute episodes of arthritis were associated with erythema nodosum, suggesting an allergic basis.

S. MATTINGLY

Peptic Ulceration Associated with Prednisolone Therapy. K. T. EVANS. *Brit. J. Radiol.*, 1958, **31**, 307.

Barium-meal examinations were carried out on 23 patients being treated with prednisolone for various medical conditions, 13 of them having rheumatoid arthritis. The average dose was 20 mg. daily.

Peptic ulceration was found in six cases, and five of these had rheumatoid arthritis. In two instances there were no symptoms, and healing took place without stopping prednisolone treatment. The ulcers demonstrated were either pre-pyloric or in the duodenal cap, generally very large and unlike the type usually seen.

Most of the patients were given alkalis in view of the suspected risk of peptic ulceration, but this did not affect the incidence.

MAURICE F. HART

Intra-articular Hydrocortisone in High Concentration. B. M. NORCROSS. *J. Amer. med. Ass.*, 1958, **167**, 839.

In treating rheumatoid arthritis and osteoarthritis it was found that injections into large joints of 150–300 mg. of hydrocortisone acetate produced better results than doses of 25–50 mg. The relief of pain was greater and the effect lasted longer.

D. A. BREWERTON

Reflex Sympathetic Dystrophy. F. M. O'CONNOR. *A.M.A. Arch. Derm.*, 1958, **78**, 314.

A case of reflex sympathetic dystrophy which responded quickly and favourably to treatment after the condition had been established for several months is reported. The aetiology of this condition is discussed, and an attempt is made to correlate treatment with the degree of disordered physiology. The author suggests that different degrees of sympathetic block are needed for differing degrees of disorder. The technique of sympathetic block is not discussed, but a good bibliography is given.

D. C. ARNOTT

The Speed of Healing after Fracture of the Tibial Shaft. H. ELLIS. *J. Bone Jt Surg.*, 1958, **40B**, 42.

Disabilities after Tibial Shaft Fractures. H. ELLIS. *J. Bone Jt Surg.*, 1958, **40B**, 190.

These two papers from the Royal Infirmary, Sheffield, comprise an analysis of the factors affecting clinical union in 535 fractures of the tibia, and a study of the late results of 343 soundly united tibial shaft fractures.

The author considers that the severity of the injury is probably the most important factor in determining the speed of healing and in the incidence of delayed union and non-union. Delay in healing also takes place if traction causes dis-traction. The most important cause of disability following fractures of the tibial shaft was limitation of ankle and/or foot movements. Residual stiffness of the foot was correlated with the severity of the injury. One-third of the patients with limitation of foot and ankle movements had clinical evidence of ischaemic contracture. The author believes that this may result from either direct tissue damage or associated vascular damage.

P. J. R. NICHOLS

De Quervain's Disease. L. LEAO. *J. Bone Jt Surg.*, 1958, **40A**, 1063.

The first part of this paper reports the findings of dissections of 50 wrists of 27 fresh cadavera and emphasizes the frequency of variation in the structures forming the anatomical snuff-box. The second part of the paper is a review of 32 cases of de Quervain's disease in 29 patients, nine of which were treated by operation. Although the condition is apparently self-limiting (two patients who refused treatment were free of symptoms when reviewed), conservative treatment, whether by hydrocortisone, analgesic drugs, or immobilization, is usually lengthy. Operation gives a quick and reliable cure.

P. J. R. NICHOLS

Recent Advances in Local Anesthesia. E. A. SNEDDON. *Med. Clin. N. Amer.*, 1958, **42**, 1239.

The properties required in an ideal local anaesthetic are set down, and the author attempts to relate various recently introduced substances to these criteria. Reactions to local anaesthetics are divided into three categories: (1) due to a high blood level of the anaesthetic; (2) due to abnormal response by the patient; and (3) associated reactions due to the inclusion of a vasopressor drug. Treatment of these abnormal reactions is discussed. Maximum doses of various anaesthetics are given. The properties of procaine and Xylocaine and the effect of the inclusion of hyaluronidase are described, and guidance is given for the safe administration of local anaesthetics. The danger of rapid absorption of local anaesthetic from the epidural space is emphasized.

D. C. ARNOTT

"Durafoam"—a New Material for Rest Splints in the Prevention of Deformity in the Chronic Rheumatic Diseases. J. N. SWANSON. *Canad. med. Ass. J.*, 1958, **79**, 638.

A new material for splint-making and the technique of its application are described. Among the advantages of this material the following appear to constitute real advances: (1) it is light, strong, washable, and waterproof; (2) it can be made when and where it is required by the interaction of two chemicals; (3) the heat generated by the chemical process is slight, allowing splints to be moulded directly to the skin; (4) splints made from this material are easily trimmed; (5) it is transparent to X rays, and is unaffected by oil, ointment, alcohol, or secretions; (6) it is non-inflammable; (7) it does not cause allergic reactions and is non-toxic; (8) it can be heated and remoulded under an infra-red lamp; and (9) different colours are available.

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D. C. ARNOTT

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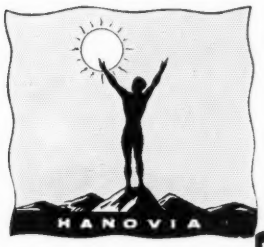

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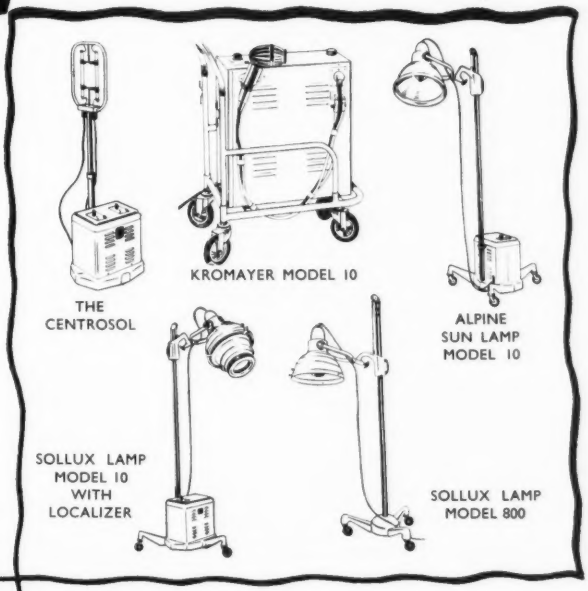

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